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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/627,896	07/27/2000	Man Sung Co	GNN-5315DV1	2462

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EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 12/30/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

BEST AVAILABLE COPY

Office Action Summary

Application No.

09/627896

Applicant(s)

Examiner

GAMBEL

Art Unit

1644

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.138(e). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on _____.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) _____ is/are pending in the application. 1-26
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration. 5
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) _____ is/are rejected. 1-24, 6-26
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 7/26/01 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

U.S. Patent and Trademark Office
PTO-328 (Rev. 04-01)

Office Action Summary

Part of Paper No. 19

PAPER No. 19

DETAILED ACTION

1. Applicant's amendment, filed 7/26/02 (Paper No. 14), has been entered.
Claims 1-3 have been amended.
Claims 6-26 have been added.

Applicant's amendment, filed 10/11/02 (Paper No. 17), has been entered
Claims 9, 15 and 21 have been amended.

Claims 1-4 and 6-26 are being acted upon as they read on the elected invention.

Claim 5 has been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to nonelected invention

2. Formal drawings, filed 7/26/02, have been submitted which comply with 37 CFR 1.84.
3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. The amendment, filed 10/11/02 (Paper No. 17), is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.
The added material which is not supported by the original disclosure is as follows:
"The entire nucleotide and amino acid sequences for the 3D1 in the Sequence Listing, filed 10/11/02 (Paper No. 17).

It appears that the application as filed provides written support for the nucleotide and amino acid sequences for the variable domains of the 3D1 antibody and does not provide written support for the nucleotide and amino acid sequences for the entire 3D1 antibody.

Applicant is required to cancel the new matter in the reply to this Office Action.

Alternatively, applicant is required to provide clearer direction from the specification as filed for the additional nucleotide and amino acid sequences disclosed in the Sequence Listing.

5. Claims 1-4 and 6-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-4 and 6-26: It is apparent that the "3D1" and "H2F", "I2R" antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell lines/hybridomas which produces these antibodies. See 37 CFR 1.801-1.809.

Applicant asserts that only the amino acid sequence from the framework regions of the I12R and H2F antibodies are required to be disclosed to one of ordinary skill in the art and notes that these sequences are available in Manheimer-Lory et al., J. Exp. Med. 174: 1639-1652 (1991).

Applicant's comments on the construction of the disclosed humanized B7-2-specific antibodies are understood.

However, the claims recite and, in turn, require the "3D1" and "H2F", "I2R" antibodies to enable the claimed invention. Therefore, the claims should recite either the appropriate deposit information (Accession Numbers) and/or SEQ ID NOS for "3D1" and "H2F", "I2R" antibodies.

Applicant's submission of the entire nucleotide and amino acid sequences for the 3D1 antibody in paper form, filed 10/11/02 (Paper No. 17), is acknowledged. However, it appears that the application as-filed does not support the written description of the entire nucleotide and/or amino acid sequences of 3D1 antibody. Therefore, these additional sequences provided in the Sequence Listing, filed 10/11/02 (Paper No. 17), is considered new matter for the reasons above. Again, the claims do not recite the appropriate deposit information (Accession Numbers) and/or SEQ ID NOS for "3D1".

Further, biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question from a given depository prior to and after the filing date of the application does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public. The applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from the depository, nor is there any evidence as to the depository's policy regarding the material if a patent would be granted. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. In the absence of evidence that the "3D1", "H2F" and "I2R" antibodies / hybridomas are readily available to the public and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, applicant's arguments are not persuasive and the rejection is maintained.

It is noted that the mere reference to a deposit or the biological material itself in any document or publication does not necessarily mean that the deposited biological material is readily available. Even a deposit made under the Budapest Treaty and referenced in a United States or foreign patent document would not necessarily meet the test for known and readily available unless the deposit was made under conditions that are consistent with those specified in these rules, including the provision that requires, with one possible exception, that all restrictions on the accessibility be irrevocably removed by the applicant upon the granting of the patent. Ex parte Hildebrand, 15 USPQ2d 1662 (Bd Pat. App. & Int. 1990). See MPEP 2404.01

As pointed out previously, in addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

It is noted that if the claimed and disclosed amino acid sequences or nucleic acid sequences set forth in the instant application encode the entire "3D1", "H2F" and "I2R" antibodies; then a deposit for said "antibodies (cell lines/hybridomas) is not required. The sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. However, the specification as filed must provide sufficient written description for the entire immunoglobulin to avoid new matter concerns.

The 3D1 Antibody

Applicant's assertion that the submission of the entire nucleotide and amino acid sequences for the 3D1 antibody in paper form, filed 10/11/02 (Paper No. 17), thereby making the antibody available to the public is acknowledged.

However, the application as-filed did not provide sufficient written description for the entire nucleotide and amino acid sequence of the 3D1 antibody. Therefore, applicant cannot rely upon information not supported by the specification as-filed to provide essential material to enable the claimed invention.

It appears that the application as-filed provides for the sequences of the variable (Figures 1A-B, 2A-B) but not the constant regions of the humanized and murine 3D1 antibodies.

Alternatively, it does not appear that the 3D1 antibody has been deposited under the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

The I2R (III2R) and H2F Antibodies

Applicant's reliance on the availability of the sequences for the III2R and H2F antibodies in *Manheimer-Lory*, J. Exp. Med. 174: 1639-1652 (1991) is acknowledged.

However, it appears that applicant is attempting to incorporate essentially subject matter by reference to a publication.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. *Ex parte Schwarze*, 151 USPQ 426 (Bd. of Appeals, 1966). an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See *In re Fouche*, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

If supported by the specification as-filed, applicant is invited to consider providing the sequences of the III2R and H2F antibodies and amending the specification and Sequence Listing accordingly.

Applicant is reminded of the Sequence Rules for application which contain sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825.

Applicant is also reminded of providing a Hawkins Declaration stating that the amendatory material consists of the same material incorporated by reference in the referencing application and that no new matter is being amended.

Applicant's comments on the construction of the chimeric and humanized 3D1 antibodies disclosed in the specification as-filed are acknowledged.

Although applicant asserts that the III2R and H2F antibodies themselves were never physically used as reagents and that it is not necessary for the entire amino acids of these antibodies and hybridomas that produced these antibodies to be disclosed, the claims recite 3D1, III2R and H2F as reference or starting materials in the claimed invention. Therefore, the 3D1, III2R and H2F antibodies (and/or hybridomas) are required to practice the claimed invention and are considered essential to the claimed invention.

Therefore, applicant must provide the sequences in compliance with the Sequence Rules and/or deposit the appropriate biological materials to satisfy the enablement requirements under 35 USC 112, first paragraph in order for the skilled artisan to make and use the claimed invention.

Again applicant is invited to consider incorporation by reference or the deposit of the appropriate biological materials as indicated above and of record. Applicant is reminded that the specification as-filed must provide adequate written support if applicant intends to amend the application to bring in sequences not disclosed in the application as-filed to avoid new matter considerations.

6. Claims 1-4 and 6-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 and 6-26 are indefinite in the recitation of "3D1" and "H2F", "I2R" antibodies because their characteristics are not known. The use of "3D1" and "H2F", "I2R" antibodies" as the sole means of identifying the claimed antibodies renders the claims indefinite because these "names" are merely laboratory designations which do not clearly define the claimed products; since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas. There are many subjective and objective characteristics that can be associated with an antibody, including the 3D1" and "H2F", "I2R" antibodies. In addition, a particular biological cell line such as a hybridoma can undergo changes resulting in microheterogeneity in the products such as antibodies that such cell lines can reproduce.

To obviate any ambiguity as to whether the designations 3D1" and "H2F", "I2R" antibodies refers to a particular characteristic (e.g. B7-2-specificity) , to a particular set of characteristics (e.g. structural and/or functional) or to a particular cell line (e.g. ATCC HB 11686) and all of its corresponding characteristics; the recitation of the deposit cell line is required. The 3D1" and "H2F", "I2R" designations are an incomplete and ambiguous description of the biological materials in the absence of the appropriate deposit accession numbers .

As pointed out above; the disclosure of the sequence for an entire immunoglobulin satisfies the biological deposit of said immunoglobulin and amending the claims to incorporate the appropriate SEQ ID NOS. would render the claims definite.

Applicant's reliance upon the 3D1, H2F and I2R disclosed in the specification and in U.S. Patent No. 6,084,067 and Manheimer-Lory et al. (J. Exp. Med. 174: 1639-1652, 1991) antibody is acknowledged.

Applicant's arguments, filed 10/11/02 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the sequences of the 3D1 have been provided and that it is not necessary for the public to know the complete characteristics for the H2F and I2R antibodies because the framework regions were disclosed in Manheimer-Lory.

However, the claims must particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the reasons of record and reiterated herein, the claims should provide either the sequence or the appropriate deposit accession number that corresponds to the claimed biological materials.

Applicant's arguments are not found persuasive.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-4 and 6-26 are rejected under 35 U.S.C. § 103 as being unpatentable over Freeman et al. (U.S. Patent No. 6,130,316) in view of art known gene cloning and expression strategies for deriving recombinant antibodies and fragments thereof, as disclosed/admitted on pages 10-28 or Examples I (only indicated as Exemplification on page 34 of the specification) Examples II/III of the instant specification or as cited by references on the 1449, as evidenced by Queen et al. (U.S. Patent No. 5,585,089)(1449; #AB) and as evidenced by Harlow and Lane (Eds., Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory 1988, Chapter 3, pages 23-35).

Freeman et al. teach the use of B7-2-specific antibodies, including recombinant antibodies thereof (columns 25-28), in order to cause immunosuppression or induce tolerance, including their use to inhibit transplant rejection in various modalities (columns 28-32). Freeman et al. teach the HF2.3D1 antibody that appears to be same B7-2-specific antibody of the instant application (see columns 27-31, Molecular Probes and columns 61-64, Example 8). In addition, Freeman et al. teach the use of inhibitory B7-2-specific antibodies in combination with other immunosuppressive reagents (columns 28-32).

It would have been have been a matter of routine experimentation well within the ordinary skill level of art to generate chimeric, humanized or recombinant HF2.3D1-/B7-2-specific antibodies, given the HF2.3D1 antibody and hybridoma and its associated properties known in the prior art. One of ordinary skill in the art would have been motivated to employ said ordinary skill level of art to generate chimeric, humanized or recombinant, given the properties of these antibodies to reduce the B7/CD28 costimulatory signaling of T cell proliferation (see columns 63-64).

It appears that applicant has relied upon the selection of the III2R and H2F framework modifications of the B7-2-specific humanized antibodies based upon the B7-2-specific 3D1 antibody, as disclosed in Example 2 of the instant specification.

For example, page 36, paragraph 1 discloses that the "The computer programs ABMOD and ENCODE (Levitt et al. J. Mol. Biol. 168: 595 (1983)) were used to construct a molecular model of the 3D1 variable domain which was used to locate the amino acids in the 3D1 framework that are close enough to the CDRs to potentially interact with them. To design the humanized 3D1 heavy and light chain variable regions, the CDRs from the mouse 3D1 heavy chain were grafted into the framework regions of the human I2R heavy chain and the CDRs from the mouse 3D1 light chain grafted into the framework regions of the human H2F light chain. At framework positions where the computer model suggested significant contact with the CDRs, the amino acids from the mouse antibody were substituted for the original human framework residues."

As indicated above, it appears that the instant "3D1" is the same as the "HF2.3D1" B7-2-specific antibody of the prior art Freeman et al. Patent.

This Freeman et al. reference differs from the instant invention by not disclosing the particular amino acid or nucleic acids of the HF2.3D1/ 3D1 antibody, nor of the particular "H2F", "I2R" antibodies and the "CRL-12524 cell line per se.

However, as clearly taught by Freeman et al.; it was obvious to one of ordinary skill in the art at the time the invention was made to humanize various antibodies, including "HF2.3D1" B7-2-specific antibody, particularly in view of its specificity and functional properties known at the time the invention was made.

Given the availability of the HF2.3D1/ 3D1 antibody and hybridoma together to others with general immunoglobulin gene cloning and expression strategies, it would have been a matter of routine experimentation well within the ordinary skill level of art to generate chimeric or humanized HF2.3D1/ 3D1 antibody B7-2-specific antibodies, nucleic acids encoding said antibodies, vectors, host cells, methods of making and compositions thereof. Given the highly conserved nature of immunoglobulin gene organization and structure and the availability of probes and PCR primers for immunoglobulin gene cloning, one of ordinary skill in the art could have isolated the functionally rearranged heavy and light chain variable regions from the HF2.3D1 hybridoma cell line and determined their sequences with a complete expectation of success. For example, the ordinary artisan does not need to determine the amino acid sequences of a rearranged V (variable) region before cloning. The claims do not differ unexpectedly or unobviously from what one of ordinary skill in the art would have expected to obtain given the known HF2.3D1 hybridoma thereof, the known heavy and light chain and the art known techniques regarding the production of chimeric antibodies, as acknowledged by the number of available art known procedures disclosed in the instant specification and cited on the Information Disclosure Statement. The claimed DNA sequences must encode a recombinant antibody comprising heavy and/or light chain variable regions of the instant B7-2-specific antibodies.

It is noted Examples 1/II/III of the specification discloses that the design of the instant "3D1", "H2F", "I2R" antibodies and the "CRL-12524 cell line were humanized versions (and associated nucleic acids, vectors, hosts cells) of the "3D1"/B7-2-specific antibody. Furthermore, it is acknowledged that the modifications of "3D1" antibody were designed on known parameters, techniques and computer programs (ABMOD and ENCODE) at the time the invention was made (also see 1449 references), including modifications to the framework regions to allow the recombinant antibodies to maintain substantial affinity to B7-2. Therefore, the claims limitations were expected functional products and modifications of making and preparing humanized HF2.3D1 /B7-2-specific antibodies at the time the invention was made.

Immunoglobulin gene structure and organization were well understood in the art at the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs encoding immunoglobulin variable regions. In addition, it was known at the time the invention was made that the benefits of producing recombinant antibodies to reduce the immunogenicity of therapeutic and diagnostic antibodies in human patients.

Queen et al. teach the improved methods of humanizing antibodies of interest with binding affinities of at least about 10^8 M^{-1} , preferentially 10^9 M^{-1} to 10^{10} M^{-1} or stronger (see entire document, including the first paragraph of the Detailed Description of the Invention on column 10). Queen et al. also the same or nearly the same methods of generating humanized antibodies with the reliance on computer modeling and modifications to the framework to select for antibodies of sufficient or high affinity for the antigen of interest at the time the invention was made (see Detailed Description of the Invention).

Also, it is noted that Harlow and Lane disclose that 10^7 M^{-1} is considered a weak signal in comparison to affinities of 10^8 M^{-1} or higher (see Table 3.1 on page 28).

Given the motivation and expectation of success in generating antibodies, including diagnostic and therapeutic antibodies to antigens of interest, including B7-2, as taught by Freeman; one of ordinary skill in the art would have had a reasonable expectation of success and motivation in generating antibodies of sufficient affinity binding, including affinities of at least about 10^8 M^{-1} , preferentially 10^9 M^{-1} to 10^{10} M^{-1} or stronger, as taught by Queen et al., to achieve such endpoints or therapeutic goals

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and admitted prior art, especially in the absence of evidence to the contrary.

Applicant's assertions that the binding affinity of at least about 10^7 M^{-1} is comparable to that of the native antibody, which is not commonly known to the one of ordinary skill in the art and applicant's arguments in combination with certain references asserts that the art recognized that the prior humanized antibodies generally lost much of their binding specificity are acknowledged.

However, these arguments are found persuasive for the reasons set forth above which provide sufficient evidence and expectation of success in deriving recombinant antibodies 10^8 M⁻¹, preferentially 10^9 M⁻¹ to 10^{10} M⁻¹ or stronger at the time the invention was made

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.



Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
December 26, 2002